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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of D. Brown et al. Art Unit 1625
Serial No. 09/839,424
Filed April 20, 2001
Confirmation No. 1761
For 2-FLUOROBENZENESULFONYL COMPOUNDS FOR THE TREATMENT OF INFLAMMATION
Examiner B. Robinson

March 19, 2003

RESPONSE TO OFFICE ACTION

TO THE ASSISTANT COMMISSIONER FOR PATENTS,

SIR:

In response to the Office action dated November 20, 2002, the time for response to which has been extended to March 19, 2003, by the payment of the fee required by 37 CFR 1.17 (check enclosed), please consider the following remarks.

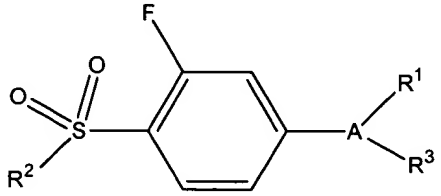
As a preliminary matter, Applicants note that copies of the references listed on the IDS filed December 3, 2001, and crossed out by the Examiner (see Paper No. 4), were resubmitted with the Amendment A and Response filed on April 30, 2002. However, the Office has not yet indicated whether these references have been made of record in the subject application.

Reconsideration is requested of the rejection of claims 1-8, 11-16, 31-32, 35-38, 40, 41, 92, 94, 99, 101, and 105-113 under35 U.S.C. § 112, first paragraph. The Office asserts that "the specification does not reasonably provide enablement for the radicals A equal to all 5 or 6 membered heterocyclic rings."[1] It is noted that the Office has not raised any issue with respect to enablement when A is selected to be a partially saturated or unsaturated carbocyclic ring.

[1] Office Action dated November 20, 2002 at page 3.

I. Claims 1-8, 11-16, 92, 99 and 105-113 are enabled by the specification.

Claim 1 is directed to compounds of Formula I:



or their pharmaceutically-acceptable salts, tautomers or prodrugs, wherein A is a 5- or 6-member ring substituent selected from partially saturated or unsaturated heterocyclic and carbocyclic rings, and R^1, R^2 and R^3 are as defined in the claim.

The standard for enablement is whether one of ordinary skill in the art could make or use the claimed invention from the disclosures in the application coupled with information generally available to those skilled in the art without **undue experimentation.**[2] The mere fact that some experimentation may be necessary to select and prepare compounds having a 5- or 6-membered partially saturated or unsaturated heterocyclic ring substituent not named in the specification does not render the specification non-enabling:

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art . . . The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.[3]

Furthermore, patent applicants are not required to show a specific example for every possible embodiment of the claimed

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[2] U.S. v. Teletronics, Inc., 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988).

[3] Ex parte Forman, 230 U.S.P.Q. 546, 547 (BPAI 1986); see also MPEP § 2164.06.

invention, so long as the specification and the general knowledge of the art would enable one of ordinary skill in the art to make and use the invention.[4]

In support of its assertion that the claims are not enabled by the specification, the Office alleges that "the state of the art and the level of predictability in the art cannot be predicted with any certainty beyond what specific test compounds/compositions and/or additional therapeutic agents should be used and are likely to provide productive results beyond those therapeutic compounds/compositions and/or additional therapeutic agents taught in the specification."[5] The Office further argues that "an indeterminate quantity of experimentation would be necessary to determine all potential therapeutic compounds/compositions' effects on the diseases claimed."[6]

The Office seems to be suggesting that **the amount of experimentation** is determinative. The requirement, however, is that the experimentation must not be **undue**, and thus conclusions based upon the amount of experimentation that may be necessary to practice a claimed invention is clearly contrary to law. The Office bears the burden of demonstrating that any experimentation required to practice the claimed invention is undue. The Office has failed to meet this burden.

As noted above, breadth of a claim should not be confused with a lack of enablement, and the fact that some experimentation may be required to make or use a claimed invention does not immediately render a claim non-enabled; indeed, even "a considerable amount of experimentation" is acceptable.

Furthermore, contrary to the assertion in the Office action, Applicants have provided significant direction in the practice of the invention as claimed. In the instant application, the specification provides over thirty synthetic schemes for the preparation of the fluoro-substituted benzenesulfonamides of

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[4] In re Borkowski, 164 U.S.P.Q. 642, 645 (CCPA 1970).

[5] Office action at 4.

[6] Id. at 4-5 (emphasis added).

Formula I generally, as well as for the preparation of particular classes of compounds within the scope of Formula I having a diverse range of heterocyclic groups for A, in addition to intermediates useful in their preparation.[7] Also provided are twenty-four examples illustrating the preparation of particular species within the scope of Formula I.[8] One of ordinary skill in the art, informed by the specification and equipped with an understanding of synthetic organic chemistry, could readily adapt these synthetic schemes and examples to prepare compounds within the scope of Formula I, having different heterocyclic groups for A than those specifically described in the schemes. Such adaptation is clearly within the abilities of one skilled in the art, and while some experimentation may be needed, such experimentation could be routinely performed by the skilled artisan, i.e., the adaptation could be accomplished without undue experimentation. for the foregoing reasons, claim 1 is enabled by the specification. Similarly, claims 2 and 3, which depend from claim 1, are also enabled by the specification.

Claim 4, which depends from claim 1, defines A as a 5- or 6-membered ring substituent selected from partially saturated or unsaturated carbocyclic rings. As noted above, claims 1-8, 11-16, 31-32, 35-38, 40, 41, 92, 94, 99, 101, and 105-113 were rejected because, as the Office stated, "the specification does not reasonably provide enablement for the radicals A equal to all 5 or 6 membered heterocyclic rings."[9] However, claim 4 does not define A to include any heterocyclic rings, and thus the Office has not established a basis by which claim 4 could be considered to be non-enabled. Furthermore, a specification must be taken as in compliance with the enablement requirement of § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for

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[7] See Schemes I-XXXVI.

[8] See Examples 1-24.

[9] See supra note 1.

the enabling support.[10] The Office bears the burden of establishing a *prima facie* case of non-enablement, which requires the Office to provide acceptable evidence or reasoning inconsistent with the contested statements.[11] The Office has failed to establish a *prima facie* case that claim 4 is not enabled by the specification. The specification includes two synthetic schemes, XXXII and XXXIII, which illustrate the preparation of representative carbocyclic rings. One skilled in the art could readily adapt these schemes to prepare compounds having other 5- or 6-membered carbocyclic rings. The Office has presented no evidence or reasoning inconsistent with this, and thus has not shown that claim 4 is not enabled by the specification.

Claims 5-7 and 11-16, which depend from claim 1, are enabled by the specification. These claims limit the definition of A to particular heterocyclic and carbocyclic substituents. Synthetic schemes illustrating the preparation of compounds comprising many of these moieties are provided as described above. One of ordinary skill in the art would be capable of adapting these schemes to prepare compounds having the other groups within the definition of A in claims 5-7 and 11-16 without undue experimentation. The Office has presented no evidence inconsistent with the enabling schemes provided in the specification.

Claim 8, which depends from claim 1, is enabled by the specification. In claim 8, A is selected from furanone, isoxazolyl, and pyrazolyl. The preparation of compounds having a furanone moiety are described in Schemes XXVIII and XXIX and Example 24. The preparation of compounds having an isoxazolyl moiety are described in Schemes XX-XXVII and Examples 22 and 23. The preparation of compounds having a pyrazolyl moiety are described in Schemes XV-XVIII and Examples 3-21. The Office has

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[10] See, e.g., In re Marzocchi, 439 F.2d 220, 223-4 (CCPA 1971); see also MPEP § 2164.04.

[11] Id.; see also In re Strahilevitz, 668 F.2d 1229, 1232 (CCPA 1982).

offered no reason to doubt the objective truth of these schemes and examples as enabling of claim 8, and thus has failed to establish a *prima facie* case that claim 8 is not enabled by the specification.

Claim 92 is directed to a pharmaceutical composition comprising a therapeutically-effective amount of a compound of claim 1. These pharmaceutical compositions are described in detail in the specification.[12] One skilled in the art could readily prepare such compositions, given this disclosure and the disclosure discussed above with respect to claim 1, without undue experimentation. Thus, claim 92 is enabled by the specification.

Claim 99 is directed to a method of treating inflammation comprising administering a therapeutically-effective amount of a compound of Formula I, defined as shown above for claim 1. The specification describes these methods in detail,[13] and further provides *in vitro* data regarding the COX-1 and COX-2 activities of these compounds.[14] In light of this disclosure, and for the reasons given above with respect to claim 1, claim 99, and claims 105-113, which depend from claim 99, are enabled by the specification.

For the foregoing reasons, claims 1-8, 11-16, 92, 99 and 105-113 are enabled by the specification, and thus satisfy the requirements of § 112, first paragraph.

II. Claims 31, 32, 35-38, 40, 41, 94 and 101 are enabled by the specification.

Dependent claim 31 is directed to compounds of Formula I corresponding to Formula III

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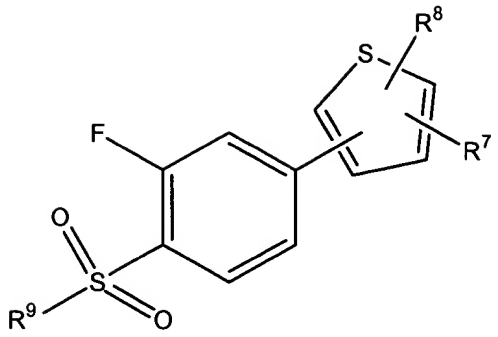
[12] See page 118, line 24 through page 121, line 23.

[13] See page 10, line 15 through page 13, line 30.

[14] See Tables 1 and 2.



or their pharmaceutically-acceptable salts, tautomers or prodrugs, wherein R^7, R^8 and R^9 are as defined in the claim. Compound of Formula III have a thiophene group which corresponds to A in Formula I.

Claim 31 is enabled by the specification. Schemes V-VII describe preparation of intermediates useful in the preparation of such thiophene-containing compounds, and Schemes VIII-XI describe the preparation of the thiophene-containing compounds themselves. Examples 1 and 2 detail the preparation and characterization of compounds within the scope of claim 31.

As noted above, a specification must be taken as in compliance with the enablement requirement of § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for the enabling support. The Office has not provided any argument to support the proposition that Schemes V-XI and Examples 1 and 2 are not enabling of claim 31. Thus, the Office has failed to set forth a *prima facie* case of non-enablement with respect to claim 31. Likewise, for the same reasons, the Office has not set forth a *prima facie* case of non-enablement with respect to claims 32, 35-38, 40, 41, or 94, all of which depend from claim 31.

Similarly, claim 101, which is directed to a method of treating inflammation comprising administering a therapeutically-effective amount of a compound of Formula III (defined as above for claim 31), is enabled by the specification. In addition to the synthetic schemes noted above (i.e., Schemes VIII-XI, which describe the preparation of compounds of Formula III), the

specification describes compounds of Formula III as COX-2 inhibitors (see, e.g., Table I and II, specifically the entries for Examples 1 and 2). Again, the Office has presented no evidence that casts doubt on the objective truth of these schemes, examples, and *in vitro* results, in light of the state of the art and the relative skill of one of ordinary skill in the art, and thus has failed to make a *prima facie* case that claim 101 does not meet the enablement requirement of § 112, first paragraph.

For the foregoing reasons, claims 31, 32, 35-38, 40, 41, 94 and 101 are enabled by the specification, and thus satisfy the requirements of § 112, first paragraph.

In view of the foregoing remarks, it is respectfully submitted that claims 1-8, 11-16, 31-32, 35-38, 40, 41, 92, 94, 99, 101, and 105-113 conform with the requirements of 35 U.S.C. § 112, first paragraph. Favorable reconsideration and early allowance of all claims are respectfully requested.

* A check in the amount of $110.00 is enclosed to cover the fee for an extension of time required by 37 CFR § 1.17. The Commissioner is hereby authorized to charge any additional fees required under § 1.17 or credit any overpayment fees to Deposit Account No. 19-1345.

Respectfully submitted,

Patricia K. Fitzsimmons, Reg. No. 52,894
SENNIGER, POWERS, LEAVITT & ROEDEL
One Metropolitan Square, 16th Floor
St. Louis, Missouri 63102
(314) 231-5400

PKF/rle

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FEE TRANSMITTAL

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Inventor(s) D. Brown et al.
Group Art Unit 1625
Examiner Name B. Robinson
Attorney Docket Number PHA 4176 (3364/1)

METHOD OF PAYMENT

1. [ ] The Commissioner is hereby authorized to charge the indicated fees to Deposit Account No. 19-1345.

   [ ] The Commissioner is hereby authorized to charge any additional fees required under 37 CFR 1.16 and 1.17 to Deposit Account No. 19-1345.

   [ ] Applicant claims small entity status.

2. [X] Check Enclosed. The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

FEE CALCULATION

1. [ ] BASIC FILING FEE Subtotal (1) $__________
   (Type: __________)

2. [ ] EXTRA CLAIM FEES Subtotal (2) $__________

   Total Claims _____
   Independent Claims _____
   Multiple Dependent Claims _____

3. [X] ADDITIONAL FEES Subtotal (3) $ 110.00

   [ ] Surcharge - late filing fee or oath
   [ ] Surcharge - late provisional filing fee or cover sheet
   [X] Extension for reply within FIRST month
   [ ] Notice of Appeal
   [ ] Filing a Brief in Support of an appeal
   [ ] Request for ex parte Reexamination
   [ ] Petitions to the Commissioner
   [ ] Submission of Information Disclosure Statement
   [ ] Recording each patent assignment per property
   [ ] Request for Continued Examination
   [ ] Other: __________

TOTAL AMOUNT OF PAYMENT $ 110.00

Patricia K. Fitzsimmons (signature)

Patricia K. Fitzsimmons, Reg. No. 52,894 — March 19, 2003 (Date)

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